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FIG. 2A

Human G Protein Coupled Receptor Family
(Receptors known as of January, 1999)

| CLASS | LIGAND | NUMBER | TISSUE | PHYSIOLOGY | THERAPEUTICS |
|---------------------------|--------|--------|--------------------------|--------------------------|--|
| •Class I | | | | | |
| Rhodopsin like | | | | | |
| •Amine | | | | | |
| •Acetylcholine | | | | | |
| •(muscarinic & nicotinic) | | 5 | Brain, Nerves, Heart | Neurotransmitter | Acuity, Alzheimer's |
| •Adrenoceptors | | | | | |
| •Alpha Adrenoceptors | | 6 | Brain, Kidney, Lung | Gluconeogenesis | Diabetes, Cardiovascular |
| •Beta Adrenoceptors | | 3 | Kidney, Heart | Muscle Contraction | Cardiovascular, Respiratory |
| •Dopamine | | 5 | Brain, Kidney, GI | Neurotransmitter | Cardiovascular, Parkinson's |
| •Histamine | | 2 | Vascular, Heart, Brain | Vascular Permeability | Anti-inflammatory, Ulcers |
| •Serotonin (5-HT) | | 16 | Most Tissues | Neurotransmitter | Depression, Insomnia, Analgesic |
| •Peptide | | | | | |
| •Angiotensin | | 2 | Vascular, Liver, Kidney | Vasoconstriction | Cardiovascular, Endocrine |
| •Bradykinin | | 1 | Liver, Blood | Vasodilation, | Anti-inflammatory, Asthma |
| •C5a-anaphylatoxin | | 1 | Blood | Immune System | Anti-inflammatory |
| •Fmet-leu-phe | | 3 | Blood | Chemoattractant | Anti-inflammatory |
| •Interleukin-8 | | 1 | Blood | Chemoattractant | Anti-inflammatory |
| •Chemokine | | 6 | Blood | Chemoattractant | Anti-inflammatory |
| •Orexin | | 2 | Brain | Fat Metabolism | Obesity |
| •Nociceptin | | 1 | Brain | Bronchodilator, Pain | Airway Diseases, Anesthetic |
| •CCK (Gastrin) | | 2 | Gastrointestinal | Motility, Fat Absorption | Gastrointestinal, Obesity, Parkinson's |
| •Endothelin | | 2 | Heart, Bronchus, Brain | Muscle Contraction | Cardiovascular, Respiratory |
| •Melanocortin | | 5 | Kidney, Brain | Metabolic Regulation | Anti-inflammatory, Analgesics |
| •Neuropeptide Y | | 5 | Nerves, Intestine, Blood | Neurotransmitter | Behavior, Memory, Cardiovascular |
| •Neurotensin | | 1 | Brain, | CNS | Cardiovascular, Analgesic |
| •Opioid | | 3 | Brain, | CNS | Depression, Analgesic |
| •Somatostatin | | 5 | Brain, Gastrointestinal | Neurotransmitter | Oncology, Alzheimer's |

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FIG. 2B

| | | | | |
|---|----------|--------------------------------|---------------------|---------------------------------------|
| •Tachykinin (Substance P, NKA ₁) | 3 | Brain Nerves | Neurohormone | Depression, Analgesic |
| •Thrombin | 3 | Platelets, Blood Vessels | Coagulation | Anti-coagulant, Anti-inflammatory |
| •Vasopressin-like | 4 | Arteries, Heart, Bladder | Water Balance | Anti-diuretic, Diabetic Complications |
| •Galanin | 1 | Brain, Pancreas | Neurotransmitter | Analgesics, Alzheimer's |
| •Hormone protein | | | | |
| •Follicle stimulating hormone | 1 | Ovary, Testis | Endocrine | Infertility |
| •Lutropin-choriogonadotropic | 1 | Ovary, Testis | Endocrine | Infertility |
| •Thyrotropin | 1 | Thyroid | Endocrine | Thyroidism, Metabolism |
| •(Rhodopsin | | | | |
| •Opsin | 5 | Eye | Photoreception | Ophthalmic Diseases |
| •Olfactory | 4(~1000) | Nose | Smell | Olfactory Diseases |
| •Prostanoid | | | | |
| •Prostaglandin | 5 | Arterial, Gastrointestinal | Vasodilation, Pain | Cardiovascular, Analgesic |
| •Lysophosphatidic Acid | 2 | Vessels, Heart, Lung | Inflammation | Cancer, Anti-inflammatory |
| •Sphingosine-1-phosphate | 2 | Most Cells | Cell proliferation | Cancer |
| •Leukotriene | 1 | White Blood Cells, | | |
| | | Bronchus | Inflammation | Asthma, Rheumatoid Arthritis |
| •Prostacyclin | 1 | Arterial, Gastrointestinal | Platelet Regulation | Cardiovascular |
| •Thromboxane | 1 | Arterial, Bronchus | Vasoconstriction | Cardiovascular, Respiratory |
| •Nucleotide-like | | | | |
| •Adenosine | 4 | Vascular, Bronchus | Multiple Effects | Cardiovascular, Respiratory |
| •Purinoreceptors | 4 | Vascular, Platelets | Relaxes Muscle | Cardiovascular, Respiratory |
| •Cannabis 2 | Brain | Sensory Perception | Analgesics, Memory | |
| •Platelet activating factor | 1 | Most Peripheral Tissues | Inflammation | Anti-inflammatory, Anti-asthmatic |
| •Gonadotropin-releasing hormone like | | | | |
| •Gonadotropin-releasing hormone | 1 | Reproductive Organs, Pituitary | Reproduction | Prostate Cancer, Endometriosis |
| •Thyrotropin-releasing hormone | 1 | Pituitary, Brain | Thyroid Regulation | Metabolic Regulation |
| •Growth hormone-inhibiting factor | 1 | Gastrointestinal | Neuroendocrine | Oncology, Alzheimer's |
| •Melatonin | 1 | Brain, Eye, Pituitary | Neuroendocrine | Regulation of Circadian Cycle |

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FIG. 2C

| | | | |
|---|---|-------------------------------|-----------------------------------|
| •Class II | | | |
| Secretin like | | | |
| •Secretin | 1 | Gastrointestinal, Heart | Obesity, Gastrointestinal |
| •Calcitonin | 1 | Bone, Brain | Osteoporosis |
| •Corticotropin releasing factor/urocortin | 1 | Adrenal, Vascular, Brain | Stress, Mood, Obesity |
| •Gastric inhibitory peptide (GIP) | 1 | Adrenals, Fat Cells | Diabetes, Obesity |
| •Glucagon 1 | 1 | Liver, Fat Cells, Heart | Cardiovascular |
| •Glucagon-like Peptide 1 (GLP-1) | 1 | Pancreas, Stomach, Lung | Cardiovascular, Diabetes, Obesity |
| •Growth hormone-releasing hormone | 1 | Brain | Growth Regulation |
| •Parathyroid hormone | 1 | Bone, Kidney | Osteoporosis |
| •PACAP | 1 | Brain, Pancreas, Adrenals | Metabolic Regulation |
| •Vasoactive intestinal polypeptide (VIP) | 1 | Gastrointestinal | Gastrointestinal |
| •Class III | | | |
| •Metabotropic Glutamate | 7 | | |
| •GABA _B | 1 | Brain | Hearing, Vision |
| •Extracellular Calcium Sensing | 1 | Brain | Mood Disorders |
| | 1 | Parathyroid, Kidney, GI Tract | Cataracts, GI Tumors |

REPLACEMENT SHEET

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FIG 3A

G protein-coupled receptors:

(Division into Class A

Or Class B)

1. **A1 adenosine receptor [Homo sapiens].** ACCESSION AAB25533
NPIVYAF RIQKFRVTFL KIWNDFRCQ PAPPIDEDLP EERPDD
Class A (SEQ ID NO: 1)
2. **adrenergic, alpha -1B-, receptor [Homo sapiens].** ACCESSION NP_000670
npiitypc sskcfkrafv rilgcqcrgr gnmrmrr lggcaytyrp wrggslers qarkdsldds gscslgsqrt lpsaspspgy
lgrgapppe lcafpewkap gallspape ppgrgrhds gplftklit epespqtdgg asnggceaaa dvangqpgfk
smmplaggqf
Class A (SEQ ID NO: 2)
3. **adrenergic receptor alpha-2A [Homo sapiens].** ACCESSION AAG00447
npviytfn hdfirafkki lergdrkriv
Class A (SEQ ID NO: 3)
4. **alpha-2B-adrenergic receptor - human.** ACCESSION A37223
npviytfn qdfirafri lcrpwtqtaw
Class A (SEQ ID NO: 4)
5. **alpha-2C-adrenergic receptor - human.** ACCESSION A31237
npviytfn qdfirafkhi lfmrrgr q
Class A (SEQ ID NO: 5)
6. **beta-1-adrenergic receptor [Homo sapiens].** ACCESSION NP_000675
npiiyrcs pdfirafqgl locarraar rhathgdrpr asgolarpgp ppsgaasdd ddddvvgatp parilepwag
cnggaasds ssldeprpg faseakv
Class A (SEQ ID NO: 6)
7. **beta-2 adrenergic receptor.** ACCESSION P07550
npiiyrcsp dfirafqell clrrsslkay gngyssngnt 361 geqsgyhveq ekenklced lpgtedfvgh qgtvpsdnid
sqgrncstnd sll
Class A (SEQ ID NO: 7)
8. **dopamine receptor D1 [Homo sapiens].** ACCESSION NP_000785
npii yafnadfrka fstilgcyrl cpatnnaiet vsimmggaam fsshheprgs iskecnlvyl iphavgsed lkkeaaagia
rpleklspal svldydtiv slekiqpitq ngqbpt
Class A (SEQ ID NO: 8)
9. **D(2) dopamine receptor.** ACCESSION P14416
npiiyttfn icfrakfiki lhc
Class A (SEQ ID NO: 9)

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FIG 3B

10. d3 dopamine receptor - human. ACCESSION G01977
np viyttfnicf rkafikilsc
Class A (SEQ ID NO: 10)
11. dopamine receptor D4 - human. ACCESSION DYHUD4
npviyvtv fnaefrnvfr kalracc
Class A (SEQ ID NO: 11)
12. dopamine receptor D5 - human. ACCESSION DYHUD5
npviya fnadfakvfa qlgcsfhcs rtpvetvnis nelisynqdi vfhkciaaay ihmmnpnavtp gnrevdndce
egpfdrmfqi yqtspdgdpv acsvweldce geisldkitp fipmgfh
Class A (SEQ ID NO: 12)
13. muscarinic acetylcholine receptor M1 [Homo sapiens]. ACCESSION NP_000729
nrmcyal cnkafirdfr lllcrwdkr rwrkipkrpg svhrtpsrqc
Class A (SEQ ID NO: 13)
14. muscarinic acetylcholine receptor M2 [Homo sapiens]. ACCESSION NP_000730
npacy alcnatfkkt fikhllmchyk nigatr
Class A (SEQ ID NO: 14)
15. muscarinic acetylcholine receptor M3 [Homo sapiens]. ACCESSION NP_000731
n pvcyalcnkt fttfkmlll cqedkkdkrk qqyqqrqsvi fhkrapeqal
Class A (SEQ ID NO: 15)
16. muscarinic acetylcholine receptor M4 [Homo sapiens]. ACCESSION NP_000732
npa cyalcnatfk ktfihlllcq yrnigtar
Class A (SEQ ID NO: 16)
17. m5 muscarinic receptor, locus HUMACHRM ACCESSION AAA51569
npicyalcnr tfrtkfmll lcrwkkdkve eklywqgnsk lp
Class A (SEQ ID NO: 17)
18. 5-hydroxytryptamine (serotonin) receptor 1A [Homo sapiens]. ACCESSION BAA90449
npviy ayfinkdfqna fikiikckf
Class A (SEQ ID NO: 18)
19. 5-hydroxytryptamine (serotonin) receptor 1B [Homo sapiens]. ACCESSION BAA94455
npiiyt msnedfkqaf hklirfkets
Class A (SEQ ID NO: 19)
20. 5-hydroxytryptamine (serotonin) receptor 1E [Homo sapiens]. ACCESSION BAA94458
n pllytsfmed fklafkklir cre
Class A (SEQ ID NO: 20)

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FIG 3C

21. **OLFACTORY RECEPTOR 6A1. ACCESSION O95222**
 npiiyclnq evkralccil hlyqhqpdp kkgsmv
 Class A (SEQ ID NO: 21)
22. **OLFACTORY RECEPTOR 2C1. ACCESSION O95371**
 npliy tirnmevkg hrlgkgre vg
 Class A (SEQ ID NO: 22)
23. **angiotensin receptor 1 [Homo sapiens]. ACCESSION NP_033611**
 npl fyglgkckf ryflqllkyi ppkakshnl sfkmsfisy psdnvssstf kpapcfve
 Class B (SEQ ID NO: 23)
24. **angiotensin receptor 2 [Homo sapiens]. ACCESSION NP_000677**
 npflycf vgnrfqqdr svfrvpitwl qgkresmscr kssslremet fvs
 Class B (SEQ ID NO: 24)
25. **interleukin 8 receptor beta (CXCR2) [Homo sapiens]. ACCESSION NM_001557**
 NPLIYAFIGQKFRHGLLKILAIHGLISKDSLKDSRPSFVGSSSGHTSTTL
 Class B (SEQ ID NO: 25)
26. **cx3c chemokine receptor 1 (cx3cr1) (fractalkine receptor)**
 ACCESSION P49238
 np liyafagekf rrylyhlygk clavicgrsv hvdfssscsq rsrhgsvlss nfyhtadgd allil
 Class B (SEQ ID NO: 26)
27. **neurotensin receptor - human. ACCESSION S29506**
 n pilynlvsan fihiflatia clcpvwmmr krpafsrkad svssnhfss natretly
 Class B (SEQ ID NO: 27)
28. **SUBSTANCE-P RECEPTOR (SPR) (NK-1 RECEPTOR) (NK-1R). ACCESSION P25103**
 npiiyccind rfilgldhaf rocpfisagd yeglemkstr yltqgsvyk vsrlctfistvvgahcepe dgpkatpssl
 dltsncssrs dskmtesfs fssnvl
 Class B (SEQ ID NO: 28)
29. **vasopressin receptor type 2 [Homo sapiens]. ACCESSION AAD16444**
 npwiyasfss svsselrll ccargtrpps lgpqdescff asslakdts s
 Class B (SEQ ID NO: 29)
30. **thyrotropin-releasing hormone receptor - human. ACCESSION JN0708**
 npviy nlmsqkfraa frklenckqk ptekpanysv alnysvikes dhfstelddi tvtdtylsat kvsfddtola sevsfsqs
 Class B (SEQ ID NO: 30)

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FIG 3D

31. **oxytocin receptor - human. ACCESSION A55493**
npwiyw lftghlfhel vqrflccsas ylkgrlget saskksnass fvlsrshssq rscsqpsta
Class B (SEQ ID NO: 31)
32. **neuromedin U receptor [Homo sapiens]. ACCESSION AAG24793**
npvlyslmssrfretfqcclgacchrlprhshshslsmnttgstlcdvgslgswvhplagndgpeaqgetdps
Class B (SEQ ID NO: 32)
33. **gastrin receptor. ACCESSION AAC37528**
nplvy cfnhrtrfqa cletcarccp rpprarpral pdedpptpsi aslsrlytt lsdgpg
Class B (SEQ ID NO: 33)
34. **galanin receptor 3 [Homo sapiens]. ACCESSION I0879541**
nplv yalasrhfra rfrtlwpcgr nrhraral rrvpassgp pgcpgdarps grillagggqg pepregpvhg geaargpe
Class A (SEQ ID NO: 34)
35. **edg-1 - human. ACCESSION A35300**
npuiy tltnkenmra firimsccckc psqdsagkfk rpiuagmefs rsksdnsshp 361 qkdegdnpet imssgnvnss s
Class A (SEQ ID NO: 35)
36. **central cannabinoid receptor [Homo sapiens]. ACCESSION NP_057167**
npuiyalr skdlrhafis mfpscegtaq pldnsmgdsd clhkhannaa svhraaescl kstvkiaakt msvstdtsac al
Class A (SEQ ID NO: 36)
37. **delta opioid receptor - human. ACCESSION I38532**
npvlyaf ldenfkrcfr qlcrkpcgrp dpssfsrpre atarervtac tpsdggpggr aa
Class A (SEQ ID NO: 37)
38. **proteinase activated receptor 2 (PAR-2) human. ACCESSION P55085**
dpfvyyfvshdfrdhaknallcrsvrtvkqmqltskhharksssysssttvktsy
Class A (SEQ ID NO: 38)
39. **vasopressive intestinal peptide receptor (VIPR) rat. ACCESSION NM_012685**
NGEVQAELRRKWRRWHLQGVLGWSSKSQHPWGGNGATCSTQVSMLTRVSPSARR
SSSFQAEVSLV
Class B (SEQ ID NO: 39)